Acute colonic pseudo-obstruction complicating chemotherapy in paediatric oncohaematological patients: clinical and imaging features

¹G E LEE, MD, ¹G-Y LIM, MD, ²J-W LEE, MD and ²B CHO, MD

¹Department of Radiology, St Mary's Hospital, the Catholic University of Korea, Seoul, Republic of Korea, and

²Department of Pediatrics, St Mary's Hospital, the Catholic University of Korea, Seoul, Republic of Korea

Objective: Although acute colonic pseudo-obstruction (ACPO) complicating chemotherapy is still a controversial entity, it is one with which radiologists should be familiar. We describe the imaging features of ACPO in children following chemotherapy for treatment of a haematological malignancy.

Methods: We retrospectively reviewed the imaging features of eight children (age 3–14 years) with chemotherapy-related ACPO, all of whom had undergone plain radiography and CT examinations. The diagnosis of ACPO was based on both clinical features and imaging findings.

Results: Abnormalities noted on plain radiography included faecal gaseous distension of the transverse colon (4/8), faecal gaseous distension of the ascending colon (3/8), gaseous distended transverse colon (3/8) and gaseous small bowel loops (6/8). As seen on CT scans, findings of faecal fluid distended the ascending and transverse colon (5/8), faecal gas distended the transverse and ascending colon (3/8), and small bowel dilatation (5/8) and pneumatosis intestinalis (2/8) were noted. Seven of the eight patients had colonic dilatation from the caecum to the transverse colon with the transition zone near the splenic flexure.

Conclusion: In children presenting with abdominal pain and constipation following chemotherapy, imaging features of progressive colonic dilatation seen on radiography and dilatation from the caecum to the transverse colon with the transition zone near the splenic flexure, as noted on CT, are suggestive of ACPO. CT is more successful than plain radiography for evaluating this finding, particularly in colonic segments filled primarily with fluid, but CT should not be necessary for making the diagnosis as plain radiographs and clinical evaluation should be adequate.

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Acute colonic pseudo-obstruction (ACPO) is a disorder of gastrointestinal motility characterised by marked dilatation of the colon in the absence of mechanical obstruction and with combined clinical symptoms and signs. It is thought to be caused by an autonomic imbalance such as excessive sympathetic stimulation of the colon combined with suppressed parasympathetic activity [1–3]. ACPO of the colon is often mistaken, both clinically and radiologically, for other abnormal conditions such as mechanical obstruction and paralytic ileus.

ACPO is very rarely seen in children. Although the CT findings have already been reported in an adult series [4], there have only been a few paediatric literature reports on ACPO. Our study is unique in that ACPO was diagnosed in a homogeneous group of children with underlying haematological malignancies and occurred following chemotherapy.

Methods and materials

Ours was a control study performed at a single institution. Between September 2005 and December

2009, eight children (age 3–14 years, median age 7.5 years; seven boys and one girl), with a diagnosis of ACPO following chemotherapy and who had undergone plain radiography and CT of the abdomen, were included in this study. ACPO was diagnosed based on each patient's clinical background using the following criteria: clinical symptoms of bowel obstruction such as constipation, abdominal pain and distension, which developed following chemotherapy and treatment with conservative therapy. The median interval between the beginning of the last chemotherapy infusion and the onset of clinical symptoms was 11 days (2–18 days). The clinical symptoms of the eight patients improved within 2–7 days following their diagnosis through the use of conservative therapy, including discontinuation of the chemotherapy and bowel rest, although six of these patients were treated with neostigmine therapy.

The exclusion criteria included infectious colitis and any inflammatory condition recorded according to inflammatory markers such as erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) or a positive stool culture. Patients with typhlitis or pseudomembranous colitis were also excluded.

The medical records of all eight patients were retrospectively reviewed in order to identify the clinical features, including the time between the beginning of the last chemotherapy infusion and their clinical

Address correspondence to: Dr Gye-Yeon Lim, #62, St Mary's Hospital, Yeouido-dong, Yongsungpo-gu, Seoul 150-713, Republic of Korea. E-mail: shlgv@catholic.ac.kr

symptoms, chemotherapeutic agents and the clinical outcome. Abdominal radiographs obtained at the time of diagnosis were evaluated in all patients. The location and diameter of the maximally dilated segment, the presence of a transitional zone between the dilated and non-dilated colon, small bowel gas, pneumatosis intestinalis, free peritoneal air, peritoneal fluid and fold thickening were also evaluated.

All patients had CT scans of the abdomen performed within 1–2 days after undergoing plain radiography. The CT examinations (Somatom Plus; Siemens Medical Systems, Erlangen, Germany) were performed following intravenous administration of non-ionic contrast medium (Ultravist; Schering, Berlin, Germany).

In all patients, we analysed the location and diameter of the maximally dilated colon segment, the presence of a transitional zone between the dilated and non-dilated colon, small bowel dilatation, pericolic fat infiltration, mucosal fold thickening, mucosal enhancement, pneumatosis intestinalis, free peritoneal or retroperitoneal air, and peritoneal fluid. The degree of colonic distension was measured at the level of the largest diameter seen on the axial or coronal images. The presence of an intermediate transitional zone was defined as a discrepancy of 50% or more between the proximal and the distal colonic calibre with residual gas or faecal material in the distal colon. An abrupt transition zone was defined as a discrepancy of 50% or more between the proximal and distal colonic luminal calibre and complete collapse of the distal colon.

Results

All patients received vincristine infusion in a dose ranging from 0.7 to 5.2 mg (mean 2.6 mg). Vincristine was given with intrathecal methotrexate (6/8), dexamethasone (5/8), daunorubicin (3/8), asparaginase (2/8), cytarabine (2/8) and etoposide (2/8) in various combinations and in dosages used for treating acute leukaemia (7/8) and non-Hodgkin's lymphoma (1/8). Remission induction chemotherapy for acute lymphoblastic leukaemia was the most common regimen given prior to a diagnosis of ACPO.

The patient radiographic characteristics are presented in Table 1. Abnormalities noted on plain radiography included faecal gaseous distension of the transverse colon (4/8) (Figure 1a), faecal gaseous distension of the ascending colon (3/8) (Figure 1a), gaseous distended transverse colon (3/8) (Figure 1b) and small bowel gas (6/8).

On plain radiography, the mean overall maximal colonic dilatation measured approximately 5.5 cm with a diameter in the range of 4–7 cm.

The patient CT findings are summarised in Table 2.

As seen on the CT scans, findings of faecal fluid distended transverse and ascending colon (5/8) (Figure 2b,c), faecal gas distended transverse and ascending colon (3/8) (Figure 1b), and small bowel dilatation (5/8) and pneumatosis intestinalis (2/8) were noted. Seven of the eight patients had colonic dilatation from the caecum to the transverse colon with the intermediate transition zone located near the splenic flexure (Figures 1c and 2b,c).

On CT examination, the mean overall colonic dilatation, as measured at the greatest anteroposterior or transverse diameter, was 5.3 cm (range 3.9–6.2 cm) for the caecum and 4.8 cm (range 3.6–5.6 cm) for the transverse colon. There were no findings of wall thickening, pericolic infiltrates, mucosal enhancement, free peritoneal or retroperitoneal air, or peritoneal fluid in any of the patients, and no patient had complications such as perforation or peritonitis.

Discussion

ACPO is a disorder of gastrointestinal motility and is characterised by marked dilatation of the colon in the absence of mechanical obstruction; it is caused by autonomic imbalance [5]. Predisposing factors for the development of ACPO include trauma, infection, neurological disease, hypothyroidism and electrolyte imbalance as well as renal insufficiency, cancer and the effects of chemotherapy [5]. Chemotherapy also may cause severe, and sometimes life-threatening, adverse gastrointestinal reactions such as ileus, peritonitis and haemorrhage. The rapidly proliferating epithelium of the gastrointestinal tract is particularly sensitive to the cytostatic drugs used in chemotherapy. These gastrointestinal complications in paediatric oncology patients are common, especially when patients have a neutropenic status following chemotherapy.

As the interval between the last chemotherapy infusion and the onset of ACPO was approximately 2–18 days (mean, 11 days) in our study, we hypothesise that chemotherapy was a significant cause of our patients' ACPO. Although the role of each drug is difficult to determine, it has been shown that the combination of high-dosage vincristine and other drugs is strongly associated with the abnormal findings of ACPO. In addition, most of our patients were neutropenic and were

Table 1. Summary of radiographic findings in eight children with acute colonic pseudo-obstruction

Sex	Age (years)	Maximum dilated segment	Maximum diameter (cm)	Transition zone	Small bowel gas	Pneumatosis intestinalis	Fold thickening
F	9	A	7	Splenic	Present	None	None
M	4	T	4.8	None	Present	None	None
M	7	A	5.2	Splenic	None	None	None
M	10	T	4.8	Splenic	None	None	None
M	8	T	6.9	Splenic	Present	None	None
F	14	T	6.3	None	Present	None	None
M	3	T	4	Splenic	Present	None	None
M	3	T	5.3	Splenic	Present	None	None

A, ascending colon; F, female; M, male; T, transverse colon.

Figure 1. A 7-year-old boy with acute lymphocytic leukaemia experienced constipation 7 days after the start of consolidation chemotherapy with vincristine, dexamethasone, cytarabine and intrathecal methotrexate. (a) Supine radiography reveals a dilated transverse and ascending colon with amorphous faecal materials as well as normal calibre of the descending colon. (b,c) Axial CT scans show a distended transverse and ascending colon with a large amount of faecal material. The transitional zone (arrow) is seen at the splenic flexure. Pneumatosis (arrowhead) is also noted.

Table 2. Summary of CT findings in eight children with acute colonic pseudo-obstruction

Sex	Age (years)	Distension	Maximum diameter (T colon) (cm)	Maximum diameter (caecum) (cm)	Transition zone	Small bowel dilatation	Pneumatosis intestinalis	Wall thickening	Ascites	Pericolic infiltrates
F	9	Faecal	5.6	6	Splenic	Present	None	None	None	None
M	4	Fluid	4.2	5.1	None	None	None	None	None	None
M	7	Faecal	5	5.7	Splenic	Present	Present	None	None	None
M	10	Fluid	5.1	6.2	Splenic	Present	None	None	None	None
M	8	Fluid	5.2	4.5	Splenic	Present	None	None	None	None
M	14	Fluid	5.5	6.9	Splenic	None	Present	None	None	None
M	3	Fluid	3.6	3.9	Splenic	Present	None	None	None	None
M	3	Faecal	4.5	4.4	Splenic	None	None	None	None	None

F, female; M, male; T colon, transverse colon.

Figure 2. A 14-year-old boy with acute lymphoblastic leukaemia had severe constipation and abdominal pain 6 days after starting induction chemotherapy including vincristine. (a) Supine radiography shows a faecal gas distended the ascending colon with small bowel gaseous distension. (b–d) Axial (b) and coronal multiplanar reconstruction (c,d) CT scans show a distended transverse colon with an ascending colon. The lumen of the dilated colon was filled with fluid and faeces. The descending colon was not dilated (arrowhead). The transitional zone (arrow) is in the splenic flexure.

receiving broad-spectrum antibiotic therapy at the time of the diagnosis of ACPO, thus indicating that these factors are also likely to have affected the pathogenesis of ACPO.

Vincristine, which is commonly used in the management of leukaemia and selected lymphomas, has potentially neuropathic side effects [6, 7]. Sandler et al [6] reported that 46% of 50 patients receiving vincristine had abdominal pain or constipation 4–72 h following administration. However, the ACPO diagnosed in our patients could be differentiated from constipation that may develop because of neurotoxicity from vincristine,

as the neurotoxicity is dose-related and cumulative, while our study patients tended to be diagnosed with ACPO early during the course of their primary disease and did not experience symptom recurrence despite full chemotherapeutic treatment.

ACPO can be diagnosed according to patients' clinical symptoms and radiological findings. Early recognition of ACPO is important so that most patients can respond to conservative management. The initial management of ACPO has traditionally been conservative in nature and consists of nasogastric decompression, bowel rest, correction of electrolyte abnormalities, discontinuation

of drugs affecting colonic motility and treatment of any possible underlying cause [5, 8]. If no response is observed after such care, neostigmine administration may be considered as a pharmacological alternative [4, 9]. Neostigmine, a parasympathomimetic agent, is the optimal choice for managing the acute form of ACPO [5, 8, 9]. In our series, six patients with ACPO and who did not respond to initial supportive therapy were successfully treated with neostigmine.

Signs and symptoms of ACPO include abdominal distension, abdominal pain, nausea, vomiting and abdominal tenderness. Radiographically, the autonomic neuropathic expression of ACPO is acute large bowel dilatation, particularly in the transverse colon and ascending colon. However, one should have doubts if only a gaseous, dilated, transverse colon is noted on supine radiography, as it is usually prone to dilatation on supine radiography [7]. Unfortunately, age-related variations in colon size make it difficult to establish an equivalent threshold in the paediatric population. In these cases, as serial radiographs may show increasing dilatation of the transverse diameter of the colon, the relative increase in the colonic diameter compared with what is normal for a patient's age and clinical symptoms should be taken into a consideration when diagnosing ACPO.

CT is the single most useful study for obtaining important information regarding the location and cause of bowel obstruction. The CT findings in our paediatric patients indicated proximal colonic dilatation with a transitional zone at or adjacent to the splenic flexure, although structural obstructing lesions suggesting obstructive ileus were not visualised. Whereas the transition of the pseudo-obstruction seen in our cases was intermediate, that in obstructive ileus was of the acute form.

In addition, the presence of transitional colonic zones in all of our patients could be used to differentiate ACPO from paralytic ileus [4]. The location of the transitional zone can also be somewhat characteristic, as was seen in all of our patients in whom the transition zones were at the splenic flexure or adjacent to it. These findings in our paediatric series are similar to those of previous reports in adult populations with chronic ACPO [4]. Bachulis and Smith [9] reported that the transitional region in pseudo-obstruction tends to be at the splenic flexure or close to it. At the splenic flexure, the parasympathetic innervation of the colon undergoes transition from the vagal nerve for the proximal portion of the colon to the sacral nerve for the distal portion of the colon [9]. This finding may indirectly implicate an autonomic neuronal imbalance as a causative factor in colonic pseudo-obstruction and could therefore be used to differentiate it from paralytic ileus.

No other remarkable findings, such as wall thickening, pericolic infiltrates, mucosal enhancement or ascites indicating colitis, were noted in any of our patients.

Recognition of ACPO is vital for radiologists in order to prevent misinterpretation of related imaging findings and, most importantly, unnecessary procedures and surgery. As ischaemia or bowel perforation can develop as a complication of ACPO and has mortality rates greater than 50%, abdominal X-rays should be performed at least daily in order to assess the progression of ACPO and to exclude possible perforation [10].

Compared with plain abdominal films, although CT can better evaluate the presence of dilatation and a transition zone, especially in colonic segments filled primarily with fluid, CT should not generally be carried out in young patients because of its excessive radiation exposure. These concerns have led to an interest in the use of alternative imaging modalities without radiation exposure, such as MRI. Currently, MRI constitutes an important, radiation-free alternative for bowel imaging in children [11]. Although we did not obtain MR images in these studies, the decreased radiation exposure warrants further studies of this modality for evaluating paediatric patients with ACPO complicating chemotherapy.

In conclusion, although ACPO complicating chemotherapy is still a controversial entity, it is an interesting entity with which radiologists should be familiar. In our series, ACPO should be suspected if there are imaging features of progressive colonic dilatation with the transitional zone adjacent to the splenic flexure in children who present with constipation following chemotherapy. However, CT is not the preferred imaging modality for this diagnosis as plain radiographs and clinical evaluation should suffice, particularly in paediatric patients.

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